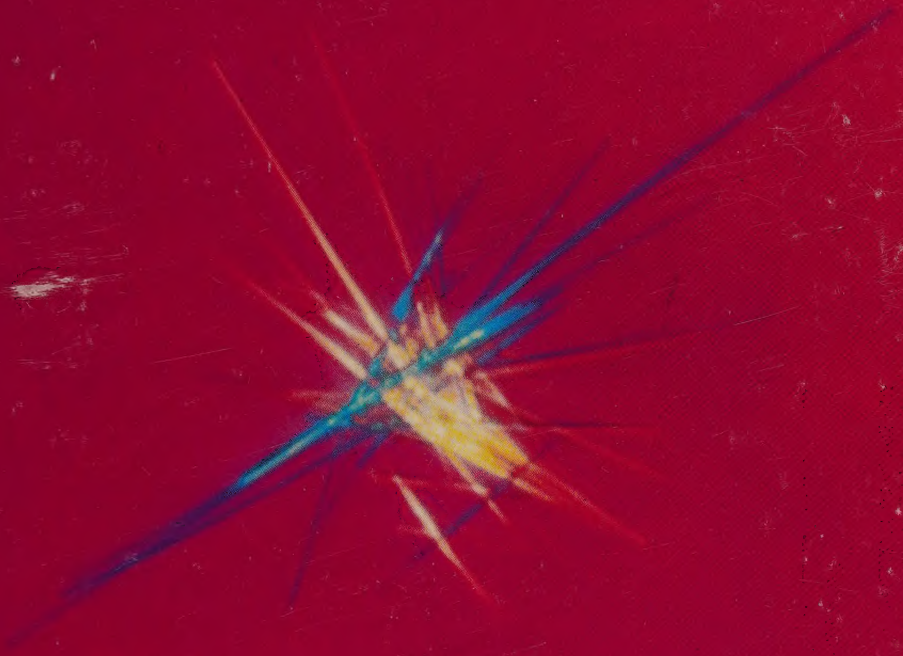




HYPERURICEMIA AND GOUT IN ORTHOPEDICS

A study on prevalence and clinical features

by

Per Henrik Widmark

Lund 1980

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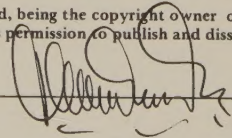
Per Henrik Widmark, Hb

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Title and subtitle Hyperuricemia and gout in orthopedics. A study on prevalence and clinical features.			
Abstract A study including approximately 3000 serum uric acid analyses and 2000 synovial fluid analyses for crystals in polarized light, was conducted on a series of patients who sought medical attention in the emergency room of an orthopedic department. The following conclusions were drawn: Hyperuricemia and gout were common in patients with arthritic symptoms, just as common as the other main type of crystal synovitis-pyrophosphate synovitis. In an unselected series of patients with a positive finding of urate crystals, men were five times as frequent as women. The age distribution appears to have changed over the years, so that today gout is a disease of the elderly. CPPD-crystal synovitis had an almost reverse female/male ratio as compared with patients with gout and/or hyperuricemia; that is men were much less represented, particularly the young men. The age and sex distribution was similar in those patients who had urate crystals and those who were suspected of having gout due to hyperuricemia. Patients with gout and patients with suspicion of gout due to a positive finding of hyperuricemia also had a similar distribution of the sites of involvement although the knee was much more often affected in those patients in whom the diagnosis had been secured by fluid analysis. In patients with knee effusion, hyperuricemia, defined as serum uric acid of 7 mg% or more, was seen in 4% of the women and 14% of the men. In the same group urate crystals were found in 5% of the women and 10% of the men. Serum uric acid agreed very well with the synovium uric acid value. Both were similarly at a higher level in patients with a positive finding of urate crystals in the synovium. There was a large overlap in uric acid values between patients who were diagnosed to have gout and the normative data. Owing to this overlap, synovial fluid analysis is a necessary requirement for the diagnosis of gout just as for the diagnosis of pyrophosphate synovitis. Moreover, both diseases, even if unrelated, appear to be about equally common.			
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Date September 18, 1980

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Malmö 1980

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In memory of my father

Erik M.P. Widmark

and

Lars Nilsson

Ebba Jönsson

Wilhelm Jönsson

The analysis of the present series of cases was undertaken because of my conviction that few diseases that are capable of being easily and accurately diagnosed are so often overlooked, or rather misinterpreted, as gout. Among well trained men gout is still too often a curiosity, rather than a clinical entity to be encountered and recognized. With the desire of centering the attention on this fact, the present study was undertaken.

Williamson (1920)

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INTRODUCTION

Large variations in the serum uric acid content and in the prevalence of hyperuricemia have been reported from various parts of the world. Studies, often referred to, have been conducted by Brøchner-Mortensen (1937), Popert and Hewitt (1962), Mikkelsen et al. (1965), Hall et al. (1967), O'Sullivan (1968, 1972), Evans et al. (1969), Isomäki (1969), Acheson and Chan (1969), Grahame and Scott (1970), Paulus et al. (1970), Thorpe and Daley (1971), Zalokar et al. (1972) and Sturge et al. (1977).

Studies with special reference to ethnic groups have yielded even more deviating results (Lennane et al. 1960, Decker et al. 1962, Ford and deMos 1964, Burch et al. 1966, O'Brien et al. 1966, Prior et al. 1966, Emmerson et al. 1969, Fahmy 1969, Healey and Jones 1971, Ibrahim 1975, Beighton et al. 1976, 1977, Yano et al. 1977, Zimmet et al. 1978, Brauer and Prior 1978).

In Sweden, data have been presented by Tibblin (1967) on 50-year-old men, by Bengtsson and Tibblin (1974) on five age samples of women, by Hedstrand (1975) on middle-aged men and by Waern (1977) on 60-year-old men.

The studies most often referred to are, however, the Tecumseh study (Mikkelsen 1965), The Framingham study (Hall 1967), the Sudbury study (O'Sullivan 1966), the Finland study (Isomäki 1969) and The Standard Oil study (Thorpe 1971).

In general, hyperuricemia is considered to be an absolute criterion for the diagnosis of gout. In recent years, survey studies on this subject have yielded very little and typical of the last decades are the following statements:

"Gout is a rare disease in Sweden" (Ask-Upmark and Adner 1950).

"Gout is very common in Denmark and Southern Sweden (Brøchner-

Mortensen 1958).

"Gout is seldom seen in the general population" (Tibblin 1972).

"Nobody of 1,462 women had gout" (Bengtsson and Tibblin 1974).

"Gout is in Sweden a unique disease" (Allander 1977).

After synovial analysis for crystals and uric acid content had been introduced in our department, it became obvious that gout, perhaps, was not such a rare disease as had been assumed in the past, particularly not in those patients who seek medical advice in an orthopedic department. In addition to the calcium pyrophosphate dihydrate crystals, which were found in joint effusions as a sign of crystal synovitis, urate crystals were found much more often than had been expected.

The aims of this study were to:

Establish the prevalence of hyperuricemia and gout in patients seen in an orthopedic department.

Describe the sex and age distribution in comparison with other sets of data.

Review the types of complaints in patients with positive findings of hyperuricemia or gout.

Investigate the relationship between clinical findings, laboratory findings and findings in microscopy of synovial fluid.

Evaluate the usefulness of fluid analysis in orthopedic patients.

MATERIAL

Normative data

The normal range of serum uric acid in the Chemistry Department or our hospital is 2 - 7 mg% in women and 3 - 8 mg% in men. For our comparative analyses, however, it was necessary to use data points obtained from individual observations in subjects covering a large age-range. For this purpose serum uric acid analysis was included in the set of standard laboratory works on all patients admitted to the Department for one complete year. Owing to various unsystematic reasons some patients escaped from having their serum uric acid measured, leaving altogether 840 women and 906 men in the age-range 15 - 97.

The obvious risk for the Berkson fallacy must be taken into consideration when using hospital data. After all, these patients were, in most instances, admitted because of locomotor malfunction. Mostly, however, they were trauma victims, patients with spine disorders or patients admitted for elective joint replacement owing to degenerative joint disease etc., but rarely patients admitted for diagnostic work on arthritis of an unknown origin. Those patients who had a serum uric acid value of 7 mg% or more, were analysed. Seven gout patients were found. Otherwise high uric acid values were associated with alcohol misuse, thiazide medication, malignant disease and nephropathia.

Patients with obvious reasons for their hyperuricemia might add significantly, if not to the average, at least to the scatter of the data, particularly in the most affected group - men over 70. However, even in this group, patients with malignant disease, alcohol misuse or gout, contributed less than 8 % of the total number. In other age groups and in women, cases with hyperuricemia were much less common and fairly evenly distributed. It was decided, therefore, that there was no ground for excluding this type of patient from the normative data in that such patients may be found in any random

sample of individuals and also since their contribution to the average and the scatter is insignificant.

Finally, the normative data were compared with data obtained from Swedish health control surveys (Table 1). In Figure 1, the range of the normative data is presented and compared with the survey data. The deviations are small and we must assume that our normative data can be used for comparisons with patients in Malmö on whom, the analysis was also carried out by the same laboratory.

Table 1. List of health surveys in Figure 1.

Source		Age	N	Mean	SD
WOMEN					
Malmö	(Trell 1980)	29	609	4.0	0.8
Malmö	(Trell 1980)	39	150	3.1	1.1
Göteborg	(Bengtsson 1974)	50	396	4.1	1.2
Göteborg	(Bengtsson 1974)	60	81	4.4	1.5
MEN					
Malmö	(Trell 1980)	29	533	5.5	1.1
Malmö	(Trell 1980)	39	65	4.8	1.3
Malmö	(Trell 1980)	48	717	5.1	1.1
Uppsala	(Waern 1977)	60	331	4.5	1.1

There is a slight skewedness to the right in the distribution of serum uric acid (Figure 2). Within the normative group, as mentioned above, there were patients with hyperuricemia which could be accounted for. Otherwise, the distribution is fairly normal and very similar to the Tecumseh data (Figure 3).

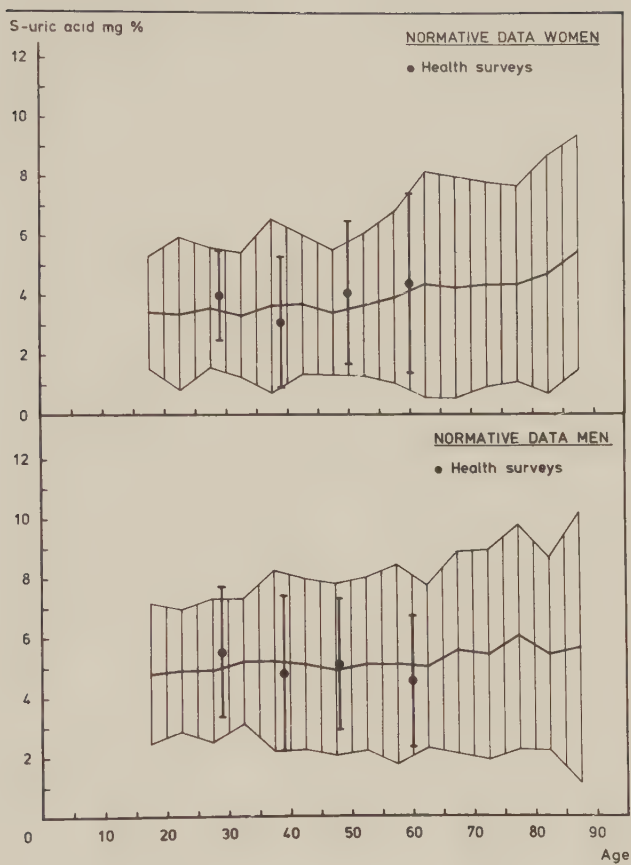


Figure 1. Normative data of serum uric acid (average and two standard deviations). Points and brackets represent health survey data from Table 1.

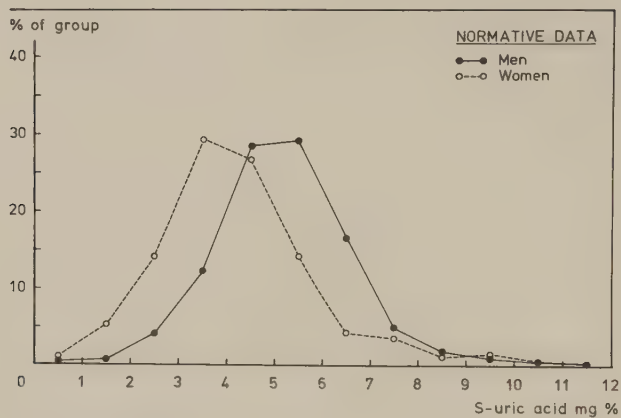


Figure 2. Distribution of serum uric acid in the normative data.

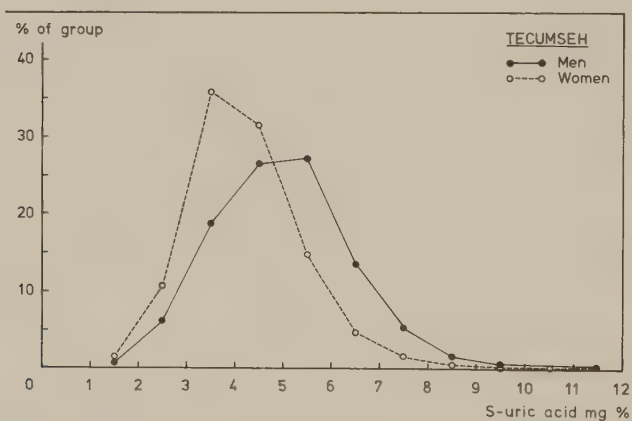


Figure 3. Distribution of serum uric acid based on the majority of the population in the town of Tecumseh, 6000 individuals.

Arthritis

Included in this group were 103 women, aged 50 ± 18 , and 156 men, aged 50 ± 17 , who were examined in the emergency room of the Orthopedic Department owing to joint complaints. In patients with such joint symptoms, a blood sample for serum uric acid analysis was taken as part of the routine procedure, even before the physical examination had been carried out and a subsequent diagnosis obtained. These were all patients who had not waited for an appointment in the out-patient clinic since they had either acute joint conditions or an exacerbation of a previous joint condition.

Knee-joint effusion

Included in this part of the study were 126 women, aged 58 ± 19 and 131 men, aged 53 ± 15 , who were seen in the emergency room owing to a knee-joint effusion and in whom serum uric acid as well as synovium uric acid analysis had been obtained. Another stipulation was that there was no history of gout, hyperuricemia or recent trauma. In 120 women and 126 men, microscopic investigation of the synovium for crystals was also undertaken.

Gout

This group includes a series of 210 patients in whom gout attacks had been verified by crystal analysis. The patients had had altogether 296 of such verified attacks. Fifty-nine of the synovia analyses were concerned with patients who were on Allopurinol* medication at the time of the attack owing to previous episodes of gout.

Hyperuricemia

In 183 patients, hyperuricemia - serum uric acid 7 mg% or more - was found in conjunction with an attack of joint symptoms which may or may not have been caused by gout. Synovial analysis was not undertaken in this group.

* Zyloric®

Pyrophosphate

In altogether 88 patients, calcium pyrophosphate dihydrate (CPPD) crystals had been found on at least one occasion in conjunction with joint symptoms. This group was investigated with respect to age and sex distribution and localization of the joint symptoms for comparison with the gout patients.

METHODS

The serum and synovium uric acid was determined spectrophotometrically after enzymatic decomposition, using the Urica Quant test kit.* The samples were taken at the time of admission to the hospital or on the arrival of the patient at the emergency room regardless of the time of day or as to whether the patient was fasting or not. The wet synovium was in all instances evaluated by the author in a microscope fitted with polarizing equipment and a first order red compensator in order to detect signs of bi-refringence (Appendix). Most of the samples were inspected shortly after the puncture and also on the following day. Only cases with obvious urate crystals were classified as gout.

The Chi-square and t-tests were used and probability levels better than 95 % have been referred to as significant.

* Boehringer & Mannheim GmbH (Kageyama 1971).

RESULTS

Serum uric acid analysis

Serum uric acid varied very little between normative data, patients with signs of arthritis and the knee effusion series (Table 2). Only in men was there a significant deviation and that only in the arthritic group. Comparing the distributions (Figures 2, 4 and 5), the similarity is obvious. Only in one set - the men in the arthritic group - was there a deviation including a skewedness to the right which, in spite of the similarity of the data otherwise, indicate the presence of a subset with high uric acid. The same may be seen in the diagrammatic representations of the individual patients in relation to age and to the normative data (Figures 6 and 7). The skewedness towards higher values is most obvious in men of the arthritic group and hardly distinguishable in any other set.

Table 2. Serum uric acid. Normative data, arthritis and knee effusion patients.

	N	Mean	SD	Per cent ≥ 7 mg%	Significance *
Normative					
Women	840	4.15	1.70	7	
Men	906	5.12	1.47	9	
Arthritis					
Women	103	3.87	1.48	3	n.s.
Men	156	5.67	1.68	22	p < 0.001
Knee effusion					
Women	126	4.06	1.49	4	n.s.
Men	131	5.33	1.50	14	n.s.

* t-test v s normative

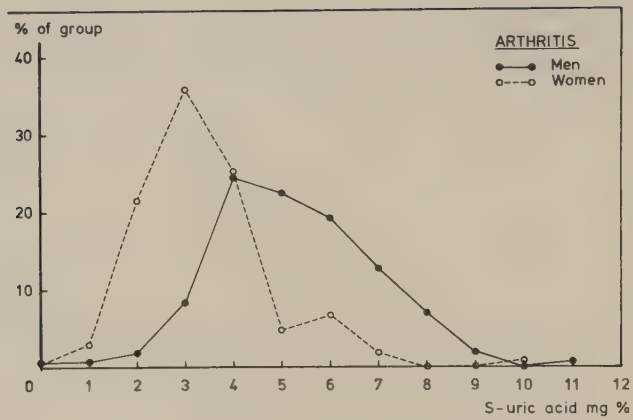


Figure 4. Distribution of serum uric acid in the arthritic cases.

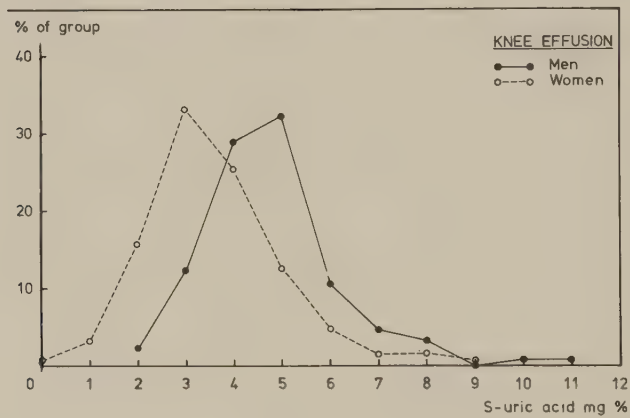


Figure 5. Distribution of serum uric acid in the knee effusion cases.

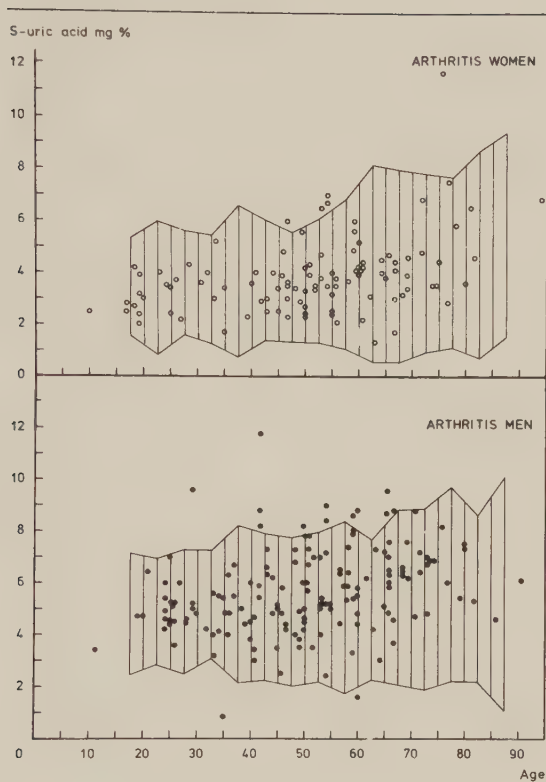


Figure 6. Individual serum uric acid values of the arthritic cases plotted on the normative data distribution and related to sex.

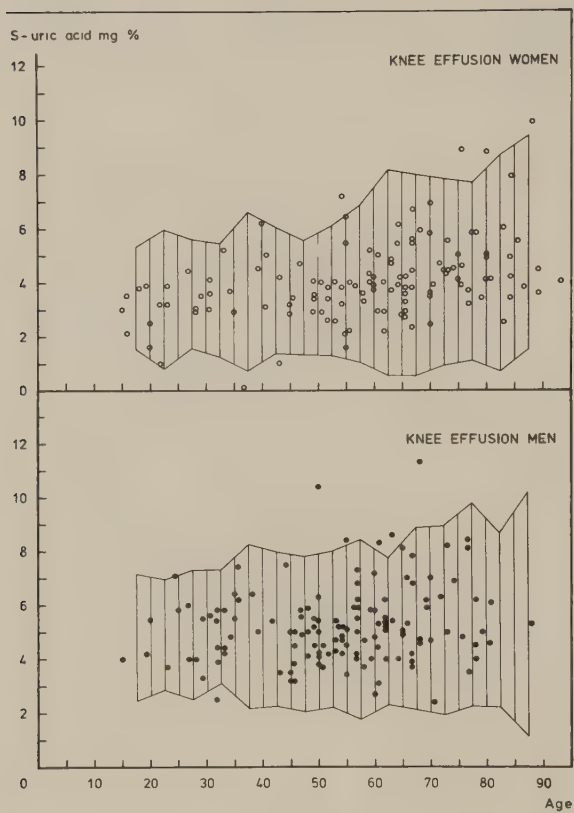


Figure 7. Individual serum uric acid values of the knee effusion cases plotted on the normative data distribution and related to sex.

Synovial fluid analysis

Altogether 66 patients of the arthritic group had a joint puncture and synovial analysis. Twelve of these patients (18%) had a positive finding of urate crystals without significant difference between the sexes in this respect; two patients had CPPD-crystals (Table 3). Among the patients with knee effusion, however, the findings of urate crystals were somewhat more rare with 5% in the women and 10% in the men. CPPD-crystals were more frequent particularly in women; the frequency of positive findings of CPPD-crystals did not differ significantly between the sexes.

Table 3. Synovial analysis in arthritis and knee-effusion.

	N	Urate crystals	CPPD crystals
Arthritis			
Women	24	4	2
Men	42	8	
Knee effusion			
Women	120	6	17
Men	126	13	14

Interaction of variables

In the knee effusion cases both serum and synovium uric acid were measured. These two variables are (Figure 8) closely related so that one may be deducted from the other with comparative accuracy. The synovium uric acid is a few tenths of mg% below serum uric acid values, similar in all concentrations. In the patients with CPPD-crystals and the patients with urate crystals the relationship between serum and synovium uric acid was the same as in the main group (Figure 9), the variables conforming to a straight line regression with considerably higher uric acid values in synovium as well as in serum for the gout patients.

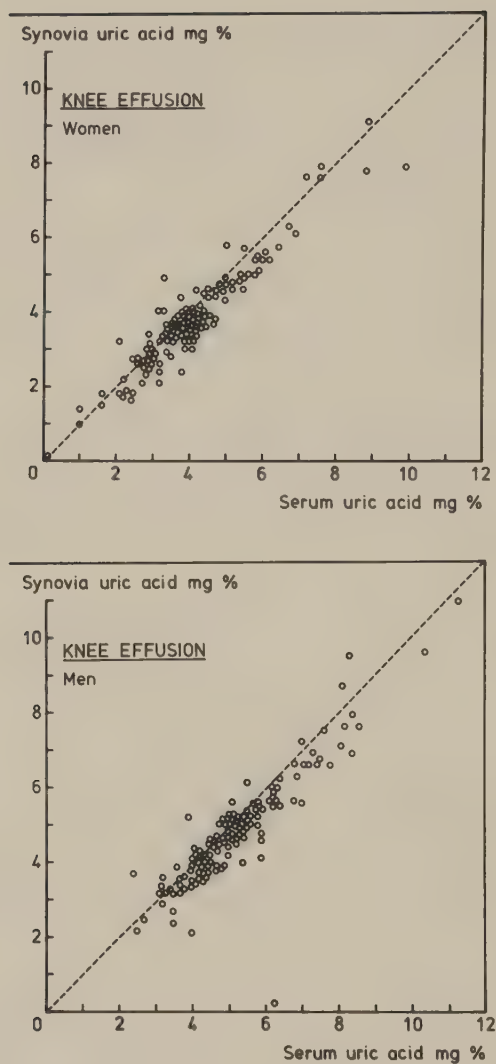


Figure 8. The relationship between synovia and serum uric acid in knee effusion patients. (Interrupted line represents the null hypothesis).

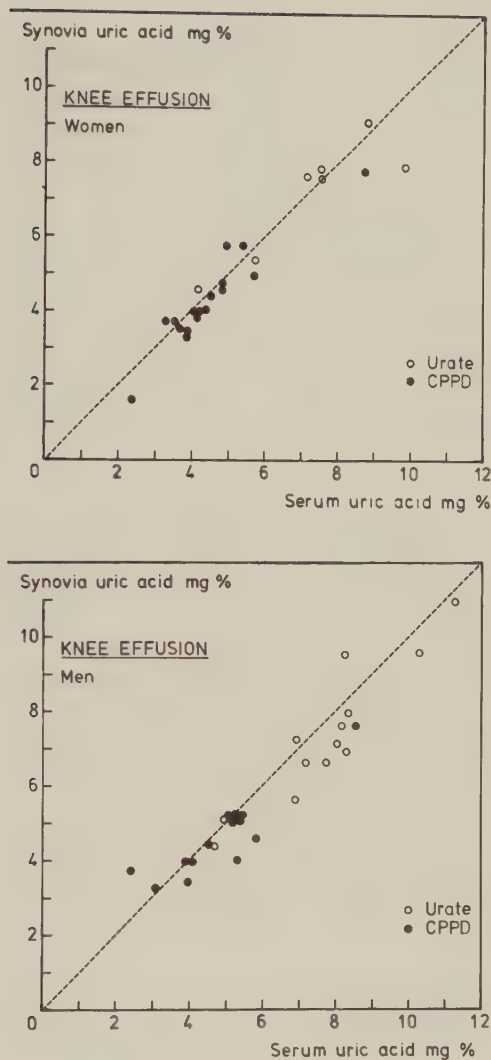


Figure 9. The relationship between synovia and serum uric acid in patients with knee effusion in cases with urate or CPPD crystals. (Interrupted line represents the null hypothesis).

Accepting values of 7 mg% or more as pathological, a substantial portion of the patients with hyperuricemia according to this criterion was only found in men (Table 2) of the arthritic group. Among those patients who had uric acid values of 7 mg% or more, the diagnosis of gout based on a positive finding of urate crystals in the analysis of the synovial fluid was found in not less than 1/4 of the cases. In the comparatively fewer knee effusion patients who had values of 7 mg% or more, the prevalence of gout as indicated by synovial urate crystals was more than 50%. In the knee effusion group, the synovium had been analysed in almost all patients but urate crystals were found in only 2% of those with a uric acid value of less than 7 mg%.

Age and sex in gout

The age and sex distributions are demonstrated in Figure 10. There is hardly any difference between the patients with proven crystal deposits - the gout patients - and those patients in whom gout may be suspected owing to hyperuricemia and joint complaints, suggesting that the two may be drawn from the same population. The female/male ratio is almost the same in the two sets and the age distributions are almost identical. In contrast to this, the sex ratio in patients with CPPD crystals is almost the reverse. The age distribution of CPPD patients deviates in one respect, namely the young men seen in the urate crystal-hyperuricemia groups are not found among the CPPD patients.

Serum uric acid in gout

There was a highly significant increase in serum uric acid in patients with urate crystals (Figure 11). However, there was also a considerable overlap between the normative data and the data of the patients with gout attacks proven by the presence of crystals. Those patients who were on Allopurinol treatment had a significant ($p < 0.001$) decrease in their uric acid values as compared with the untreated gout patients. The average difference was 1.5 mg%. The Allopurinol-treated patients

overlap to an even greater extent in their uric acid values with the normative data, half of the patients having uric acid values less than 7 mg%.

Seasonal variation of gout attacks

The frequency of diagnosed gout attacks varied somewhat with the seasons. The frequencies observed per month deviated significantly from the Poisson distribution, particularly with the low value in late summer. In Figure 12, the seasonal variations are demonstrated and variations observed in some historical data, partially in agreement with the present series, are also shown.

Sites of involvement

In Table 4, the sites of involvement are compared between gout patients, hyperuricemia patients and CPPD-patients, the CPPD-patients again deviating from the other two groups with an enormous preponderance for knee involvement.

Table 4. Sites of involvement (per cent of groups).

	Scudamore (1823)	Currie (1978)	Present study		
			Gout	Hyperuric.	CPPD
Big toe	70	59	42	25	
Small toe			1	4	
Tarsus		} 18	1	10	
Ankle	17		17	14	7
Knee	3	7	31	14	82
Finger		6	1	1	
Wrist	2	4	2	3	5
Elbow		2	1		6
Shoulder			1	5	
Other	8	4	3	24	1

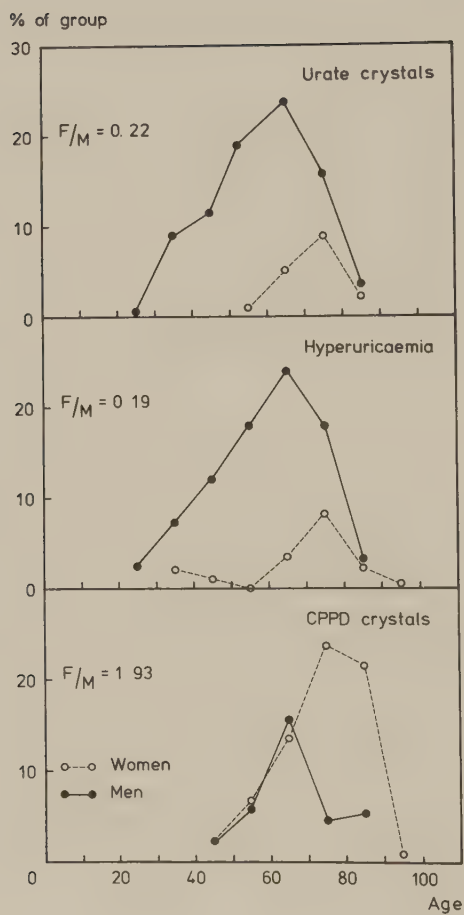


Figure 10. The age and sex distribution in patients with gout, hyperuricemia and CPPD-crystals.

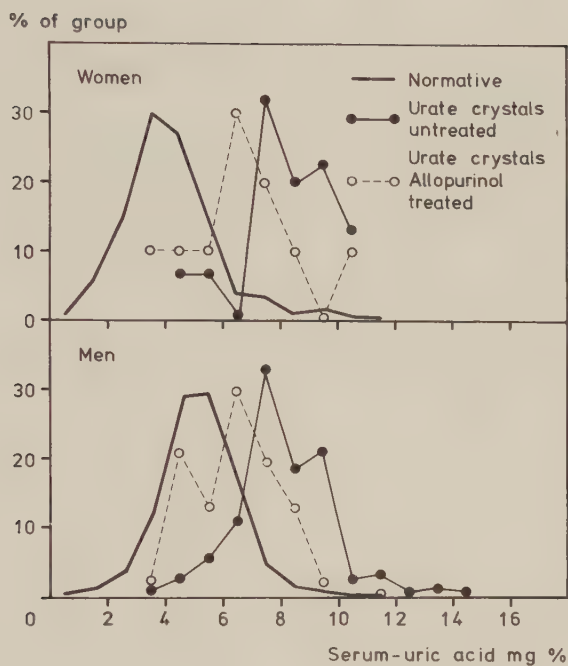


Figure 11. Distribution of serum uric acid in patients with gout as compared with the normative data. The subgroup, treated with Allopurinol, is presented separately.

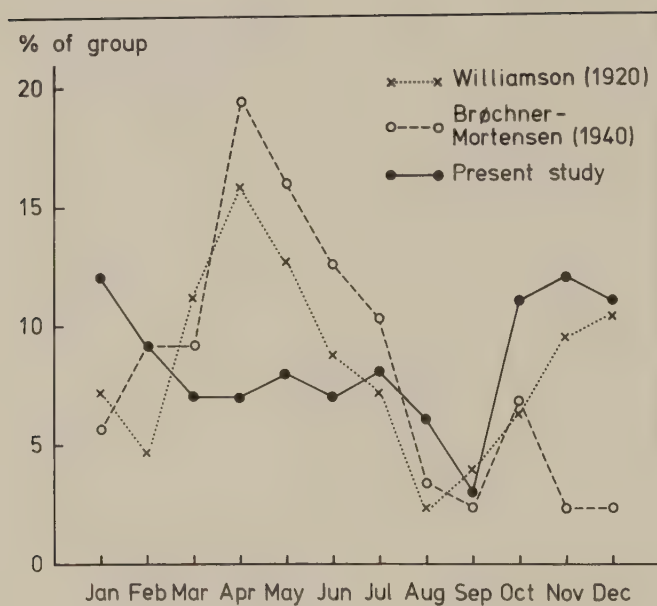


Figure 12. Seasonal variation of diagnosed gout attacks. The data of Williamson and Brøchner-Mortensen are also included.

Also, in the comparison between the gout patients and the hyperuricemia patients, there is a significant difference in that a smaller number of joints are more often involved in the gout patients. Since the diagnosis in the gout cases was based on a joint puncture with a positive finding of crystals, it is possible that a joint, known to be a site of gout such as the knee (gonagra), which is also easy to puncture and the big toe (podagra), have attracted more diagnostic efforts. In comparison with the data of Currie (1978), the most obvious difference is the fewer knee diagnoses in the Currie series, possibly due to the fact that in the latter series the cases were usually not diagnosed by joint puncture and synovial analysis. In the historical data of Scudamore, the big toe arthritis is even more predominant. These data, again, were collected at a time when neither crystal analysis nor uric acid analysis could be performed.

DISCUSSION

The prevalence of gout

The prevalence of gout varies in the literature from 0.13% (Isomäki 1969) to 10.2% (Prior et al. 1966). The data of the present study do not allow for incidental calculations. The 210 gout patients recorded who fulfilled the criteria of a positive finding of urate crystals were collected during a period of 6 1/2 years from a population of 250,000. Using the population records of the city of Malmö and calculating the incidence in those most commonly affected, men 50 - 75, one arrives at an annual incidence of first visits for gout of only 0.05%. However, in the present study a series of patients were found with hyperuricemia in conjunction with joint symptoms which partially agreed with the gout patients as regards localization and completely agreed with regard to age and sex distribution. This in itself suggests that gout is more frequent than the minimum number presented in the present study which has also included only a small part of those patients who sought medical advice in the Orthopedic Department, not to mention all those patients who were seen elsewhere. Obviously, it is not possible to draw any conclusions about the absolute incidence or even about the order of magnitude. However, our observations of the findings in the knee effusion patients and a comparison of the patients with urate crystals - hyperuricemia - with the CPPD-patients seem to indicate that gout is almost as common as pyrophosphate synovitis.

The prevalence of CPPD-crystals in this series was very similar to that of Bjelle and Sundén (1974) and Bjelle (1979, 1980) in similar studies. In comparison with pyrophosphate synovitis, there were more men in the gout series, and the men were somewhat older. The two conditions may coincide in the same patient or even in the same joint. They have it in common that they are frequently overlooked.

The circa 1/5 female/male ratio proposed by some (Kellgren et al. 1953, Prior 1962, Hall et al. 1967, Currie 1979) was supported by the findings in this study. In patients with arthritic symptoms, including the patients with knee effusions, the female/male ratio of those with gout was much larger.

It is true that gout is a rare disease; in its classical form with tophi or podagra in a middle-aged man even extremely rare. However, our efforts to improve the diagnosis by using synovial analysis has yielded many more cases so that gout, even if rare in the population at large, was found to be an important and common disease in patients with joint complaints.

Etiological factors

In the past, lead poisoning appears to have been an important cause of gout. Garrod (1859, 1876) reported that more than 25% hospitalized gout patients had saturnine gout; and Oliver (1891) pointed out that gout associated with lead poisoning was frequently found in the South of England. Lead ingested when using water from lead watering pipes, lead glazed pottery, pewter tankards, tinned cooking utensils and cosmetics appear to have been important factors which were recognized long ago. Other authors on this subject were Nordenskjöld (1772), Begbie (1862), Ludwig (1957), Emmerson (1963, 1965), Ehrlich and Chokatos (1966), Ball and Morgan (1968), Ball and Sorensen (1969), Ball (1971), Orfanos and Künzig (1975) and Campbell et al. (1977, 1978). The last authors point out that the risk for lead poisoning exists even today.

Our age distribution of patients with gout attacks differs considerably from historical data such as Scudamore (1816) who presented an average age of gout patients of less than 40. Even if this in part reflects on population distribution at that time, it by no means explains the difference from the values of today with gout as a disease mainly in the elderly (Figure 13).

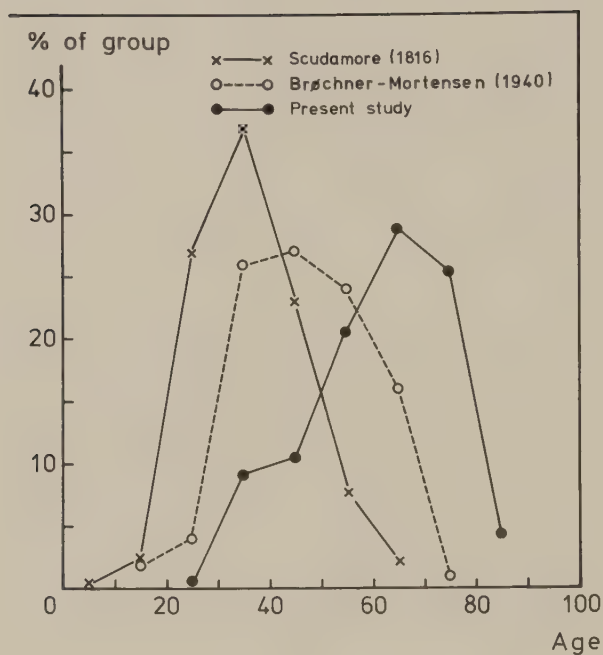


Figure 13. Age distribution 1816, 1940 and present study.

As lead disappeared as a source of intoxication, other factors have become relatively more important, such as alcoholism, use of drugs, diuretics, malignant disease and impaired kidney function (Garrod 1863, Williamson 1920, Brøchner-Mortensen 1939, 1941), Demartini 1965, Lieber 1965, Yü 1965, MacLachlan and Rodnan 1967, Evans et al. 1968, 1969, Grahame and Scott 1970, Wyngaarden 1970, Christensen et al. 1974, Bengtsson et al. 1975, Kelley 1975, Smyth 1975, Warren et al. 1975, Berglund et al. 1976, Isomäki et al. 1977). The observations of Brøchner (1941) put the age distribution somewhere between the historical data and the data of the present study. Brøchner pointed out that these patients (Danes) were mostly overweight and great consumers of beer.

The seasonal variation already observed by Hippocrates and Galen may also implicate external factors. The low rate in late summer was seen in three independent series of data. The cause of this variation remains unknown. In a contemporary British study, however, this deviation was not observed at all (Currie 1978).

Diagnosis of gout

The diagnosis of gout has in the past been based on the clinical appearance of the patient (podagra, gonagra, omagra, cheiragra), often suffering from arthritis with a vicious onset and a tendency of restoration. Serum uric acid was introduced as a diagnostic aid in gout by Folin and Denis (1912) and Folin and Macallum (1912). Since then, many workers have considered hyperuricemia a crucial criterion for the diagnosis (Garrod 1859, Talbott 1953, Gutman 1973, Boss and Seegmiller 1979). What is actually the upper normal level of serum uric acid has been discussed at length. The mean serum uric acid values vary between ethnical groups from values < 5 mg% to > 8 mg% in men and is usually 1 mg% less in women (Mikkelsen et al. 1965, Hall et al. 1967, Isomäki 1969). The saturation of monosodium urate in serum at 37° C occurs at a concentration of about 7 mg% (Klinenberg et al. 1965,

Seegmiller 1965).

For the purpose of the present study, an upper normal limit of 7 mg% was used for men as well as for women, indicating a level above which uric acid crystals are likely to precipitate and below which uric acid crystals are unlikely to precipitate. This theoretical level appears to be unimportant in relation to the actual findings in normative data as well as in patients with gout attacks. Particularly in those who had received treatment and who had a serum uric acid level not much above the average, the overlap was impressive, more than half of the patients having "normal" ($= < 7.0$ mg%) uric acid values. There are several explanations of this inconsistency. One is that the peak value which caused the precipitation of crystals may have appeared several days before the actual onset of clinical symptoms and a week or more before the analysis. Due to fluctuations in the serum uric acid level (Brøchner-Mortensen 1937), the diagnostic value of the uric acid analysis is limited. Another possible explanation is that factors other than the actual serum uric acid level are of importance for the precipitation of crystals in patients with gout as proposed by Katz (1975) and Tak et al. (1980). Allopurinol treatment, for instance, may depress the serum uric acid level (Yü and Gutman 1964, Klinenberg et al. 1965, Wyngaarden et al. 1965, Rundles et al. 1966) but still not prevent precipitation of crystals and gout attacks. If a patient on Allopurinol treatment who has a normal or even low uric acid value for weeks and months can still precipitate crystals and develop an attack of gout, possibly other, so far unknown, metabolic defects, may exist in the gout patients. This is a factor that may decrease the value of serum uric acid for the diagnosis of gout. "Hyperuricemia is a term of convenience rather than an accurate definition" (Hall 1967).

In this study it was demonstrated that a typical finding of urate crystals could be seen not only in severe gout attacks but also in patients with a single arthritis of a mild or

moderate degree. Since these patients may have had a normal uric acid value and did not live up to the classical appearance of a gout attack they will certainly not be diagnosed correctly unless synovial fluid analysis is performed. Even if hyperuricemia is a sign worth following up in a patient with joint symptoms, the synovial fluid analysis cannot be omitted. An extra benefit of this analysis is the possibility of diagnosing pyrophosphate synovitis with CPPD-crystals. Coincidence of the two is, on the other hand, comparatively rare. Only in three cases (men) included in this study were CPPD and urate crystals seen in the same synovial samples. On the other hand, a few gout patients showed CPPD crystals on later occasions. It should be remembered that, except for the classical localization, hardly any joint of the body is exempt from attacks of gout and that bursitis and tendinitis symptoms may also be due to urate crystal depositions (Fahmy 1969, Canoso and Yood 1979).

It should be noted that serum uric acid is a good measure of uric acid in the synovium. This has been demonstrated also by Friis et al. (1975). A serum uric acid, however, does not reflect the crystal state of the uric acid, neither in the synovial fluid nor in the lamina synovialis of the joint capsule.

Treatment

It is not the objective of this paper to deal with the treatment of gout. Patients encountered in the course of the study were given antiflogistics and in many instances Allopurinol in order to decrease the serum uric acid concentration in those patients who presented with severe or repeated attacks of gout. As demonstrated by Kuzell et al. (1952), Hollander (1953), Kidd et al. (1953), Hart and Boardman (1963), Smyth et al. (1963), O'Brien (1968), Cuq (1973), Wilkens and Case (1973), Widmark (1978) antiflogistics usually have a beneficial effect on gout attacks which is one important reason for arriving at a correct diagnosis. Allopurinol treatment is also

in many instances successful (Yü and Gutman 1964, Klinenberg et al. 1965, Wyngaarden et al. 1965, Delbarre et al. 1966, Hood et al. 1968, Rundles et al. 1966, Hood and Olander 1973) even if, as demonstrated in the present study, gout attacks may still occur in spite of a low level of serum uric acid. An important reason for the diagnostic work which must include microscopical analysis in polarized light is the fact that so many of the patients with gout attacks have underlying conditions which in themselves could call for treatment.

SUMMARY AND CONCLUSIONS

A study including approximately 3000 serum uric acid analyses and 2000 synovial fluid analyses for crystals in polarized light, was conducted on a series of patients who sought medical attention in the emergency room of an orthopedic department. The following conclusions were drawn:

Hyperuricemia and gout were common in patients with arthritic symptoms, just as common as the other main type of crystal synovitis - pyrophosphate synovitis.

In an unselected series of patients with a positive finding of urate crystals, men were five times as frequent as women.

The age distribution appears to have changed over the years, so that today gout is a disease of the elderly.

CPPD-crystal synovitis had an almost reverse female/male ratio as compared with patients with gout and/or hyperuricemia; that is men were much less represented, particularly the young men.

The age and sex distribution was similar in those patients who had urate crystals and those who were suspected of having gout due to hyperuricemia.

Patients with gout and patients with a suspicion of gout due to a positive finding of hyperuricemia also had a similar distribution of the sites of involvement although the knee was much more often affected in those patients in whom the diagnosis

had been secured by fluid analysis.

In patients with knee effusion, hyperuricemia, defined as serum uric acid of 7 mg% or more, was seen in 4% of the women and 14% of the men. In the same group urate crystals were found in 5% of the women and 10% of the men.

Serum uric acid agreed very well with the synovium uric acid value. Both were similarly at a higher level in patients with a positive finding of urate crystals in the synovium.

There was a large overlap in uric acid values between patients who were diagnosed to have gout and the normative data.

Owing to this overlap, synovial fluid analysis is a necessary requirement for the diagnosis of gout just as for the diagnosis of pyrophosphate synovitis. Moreover, both diseases, even if unrelated, appear to be about equally common.

CONCLUSIONS

The frequency of gout under our conditions is much greater than is commonly thought. Errors in diagnosis are relatively numerous, owing, not to the inherent difficulty in the recognition of the disease, but to the erroneous assumption of its great rarity in this country.

Williamson (1920)

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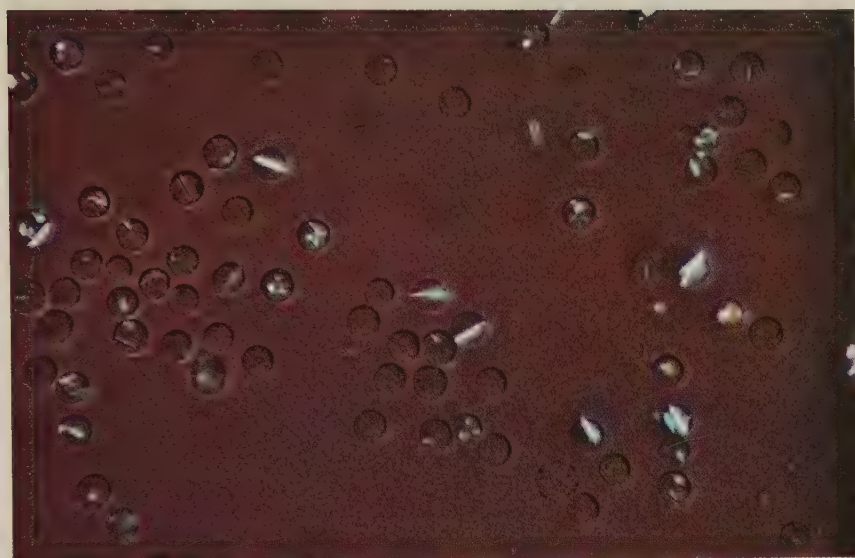
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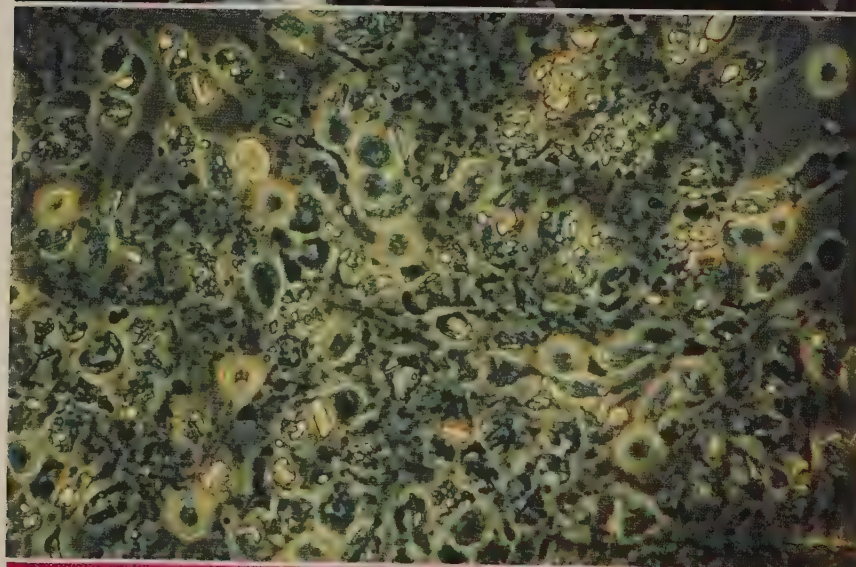
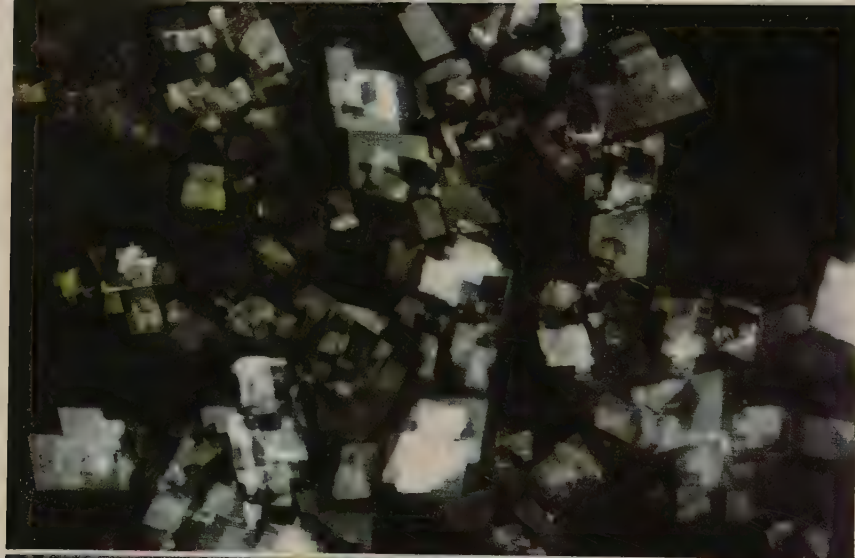
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APPENDIX

Woman, 73, with ankle arthritis and serum uric acid 9.3 mg%.
Synovia leucocyte count 7.7×10^9 /litre.
Synovia from ankle joint.
There are obvious urate crystals - intra- and extra-cellular.
(Polarized light; magnification x 500).

Man, 37, with joint complaints three days upon eating stewed liver. Serum uric acid 6.8 mg%. Synovia from podagra. Urate crystals appear as yellow or blue needles depending on their angular position in polarized light combined with a first order red compensator.
(Magnification x 500).





Cholesterol crystals.

Woman, 76, with chronic rheumatoid arthritis.

Serum uric acid 2.1 mg%. Synovia from shoulder joint.

(Polarized light; magnification x 400).

CPPD crystals.

Man, 60, with severe gonarthrosis.

Knee synovia. Various shapes of CPPD crystals.

(Phase-polaroscopy; magnification x 1000).

Cortico-steroid crystals.

Crystalline betamethason suspended in human synovia.

(Polarized light and first order red compensator; magnification x 400).

